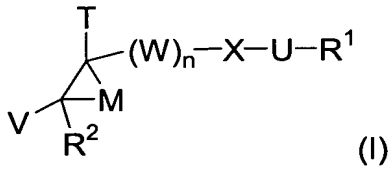
AMENDMENT OF CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1-67: (cancelled)

68. (currently amended): A method for treating or preventing an inflammatory disorder associated with TACE (TNF-α) and/or MMP, comprising administering to a subject in need thereof a therapeutically effective amount of a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt, solvate or isomer thereof, wherein:

M is $-(C(R^{30})(R^{40}))_m-$, wherein m is 1;

T is selected from the group consisting of R^{21}-substituted alkyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, $-OR^3$, $-C(O)R^4$, $-C(O)OR^3$, $-C(O)NR^{24}R^{25}$, $-C(O)NR^{24}OR^3$, $-C(O)SR^3$, $-NR^{24}R^{25}$, $-NR^{25}C(O)R^4$, $-NR^{25}C(O)OR^3$, $-NR^{25}C(O)NR^{24}R^{25}$, $-NR^{25}C(O)NR^{24}OR^3$, $-SR^3$, $-S(O)_xNR^{24}R^{25}$, $-S(O)_xNR^{25}OR^3$, -CN, $-P(O)(R^{24})(OR^{24})$, $-P(O)(OR^{24})(OR^{24})$, $-C(R^4)(=N(OR^3))$, $-C(O)$-AA-$NR^{24}R^{25}$ and $-C(O)$-AA-$NR^{25}OR^3$,

wherein each of the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl and heteroaryl groups of T is independently unsubstituted or substituted with one to five independently selected R^{20} moieties which can be the same or different, each R^{20} moiety being independently selected from the group of R^{20} moieties below;

V is selected from the group consisting of alkyl, R^{21}-substituted alkyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, $-OR^3$, $-C(O)R^4$, $-(CR^{23}R^{24})_{n1}C(O)OR^3$, $-C(O)NR^{24}R^{25}$, $-(CR^{23}R^{24})_{n1}C(O)NR^{25}OR^3$, $-C(O)SR^3$, $-NR^{24}R^{25}$, $-NR^{25}C(O)R^4$, $-NR^{25}C(O)OR^3$, $-NR^{25}C(O)NR^{24}R^{25}$, $-NR^{25}C(O)NR^{24}OR^3$, $-SR^3$, $-S(O)_xNR^{24}R^{25}$, $-S(O)_xNR^{25}OR^3$, -CN, $-P(O)(R^{24})(OR^{24})$, $-P(O)(OR^{24})(OR^{24})$, $-C(R^4)(=N(OR^3))$, $-C(O)$-AA-$NR^{24}R^{25}$ and $-C(O)$-AA-$NR^{25}OR^3$,

wherein each of the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl and heteroaryl groups of V is independently

unsubstituted or substituted with one to three independently selected R^{20} moieties which can be the same or different, each R^{20} moiety being independently selected from the group of R^{20}moieties below;

W is $-(CH_2)-$;

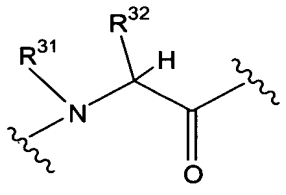
X is unsubstituted phenyl;

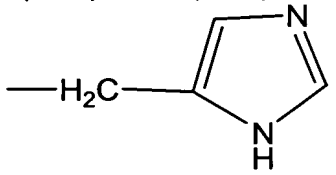
U is $-O-(CH_2)-$;

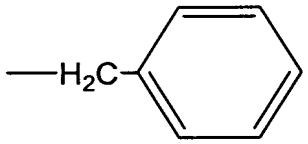
n is 0 to 2;

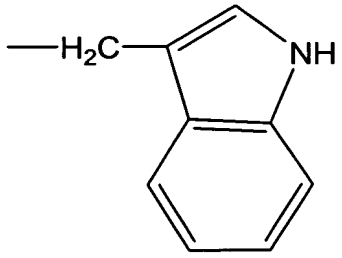
n1 is 0 to 2;

x is 0 to 2;

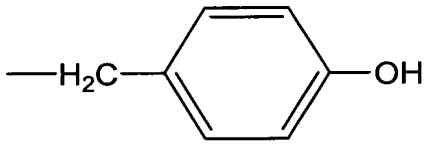
AA is  , wherein R^{31} and R^{32} are the same or different and are each independently selected from the group consisting of H, alkyl, cycloalkyl, aryl, heteroaryl, $-NR^{24}R^{25}$, $-(CH_2)_3NH(C=NH)NH_2$, $-CH_2C(O)NH_2$, $-CH_2C(O)OH$, $-CH_2SH$, $-CH_2S-SCH_2CH(NH_2)C(O)OH$, $-CH_2CH_2C(O)OH$, $-CH_2CH_2C(O)NH_2$, $-(CH_2)_4NH_2$, $-CH_2CH_2CH(OH)CH_2NH_2$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)CH_2(CH_3)$, $-CH_2CH_2SCH_3$, $-CH_2OH$, $-CH(OH)(CH_3)$,

 ,

 ,



and

 ,

or R^{31} and R^{32}, together with the N to which R^{31} is attached and the C to which R^{31} is attached, form a 5-membered ring which is unsubstituted or independently substituted with a hydroxyl group;

R^1 is selected from the group consisting of unsubstituted quinolyl, alkyl-substituted quinolyl and aryl-substituted quinolyl;

each R^2, R^4 and R^5 is the same or different and each is independently selected from the group consisting of H, halo, alkyl, R^{22}-substituted alkyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, $-OR^6$, $-C(O)R^7$, $-C(O)OR^6$, $-NR^{24}R^{25}$, $-NR^{24}C(O)R^{25}$, $-N(=C-O-NR^{24}R^{25})$,

$-NR^{24}S(O)_2R^{25}$,

wherein each of the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl and heteroaryl groups of R^2, R^4 and R^5 is independently unsubstituted or substituted with one to four independently selected alkyl, R^{22}-substituted alkyl or R^{22} moieties which can be the same or different, each R^{22} moiety being independently selected from the group of R^{22} moieties below;

each R^3 is the same or different and is independently selected from the group consisting of H, alkyl, R^{22}-substituted alkyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, $-OR^6$, $-C(O)R^7$, $-C(O)OR^6$, $-NR^{24}R^{25}$, $-NR^{24}C(O)R^{25}$, $-N(=C-O-NR^{24}R^{25})$ and $-NR^{24}S(O)_2R^{25}$,

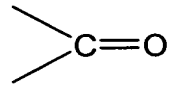
each of the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl and heteroaryl groups of R^3 is independently unsubstituted or substituted with one to four independently selected alkyl, R^{22}-substituted alkyl or R^{22} moieties which can be the same or different, each R^{22} moiety being independently selected from the group of R^{22} moieties below;

each R^6 is independently selected from the group consisting of H, alkyl and $-OCF_3$;

each R^7 is independently selected from the group consisting of H, alkyl, heteroaryl and $-CF_3$;

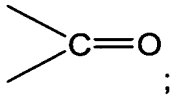
each R^{20} is independently selected from the group consisting of: alkyl, R^{21}-substituted alkyl, $-OR^3$, halo, -CN, $-NO_2$, $-NR^{24}R^{25}$, $-C(O)R^3$, $-C(O)OR^3$, $-C(O)NR^{24}R^{25}$, $-S(O)_xNR^{24}R^{25}$, $-S(O)_xR^5$, $-CF_3$, $-OCF_3$, $-CF_2CF_3$, $-C(=NOH)R^3$, aryl, halo-substituted aryl, heteroaryl, cycloalkyl, heterocycloalkyl, $-N(R^{25})S(O)_xR^5$, $-N(R^{25})C(O)R^5$, and $-N(R^{25})C(O)NR^{24}R^{25}$,

wherein each of the aryl, halo-substituted aryl, heteroaryl, cycloalkyl and heterocycloalkyl groups of R^{20} is independently unsubstituted or substituted with one to four independently selected R^{22} moieties which can be the same or different, each R^{22} moiety being independently selected from the group of R^{23} moieties below,

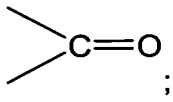
or two R^{20} groups taken together with the carbon to which both R^{20} groups are attached is  ;

R^{21} is one to three substituents independently selected from the group consisting of: $-OR^3$, halo, -CN, $-NO_2$, $-NR^{24}R^{25}$, $-C(O)R^3$, $-C(O)OR^3$, $-C(O)NR^{24}R^{25}$, $-S(O)_xNR^{24}R^{25}$, $-SO_xR^5$, $-CF_3$, $-OCF_3$, $-CF_2CF_3$, $-C(=NOH)R^3$, R^{23}-substituted alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, $-N(R^{25})S(O)_xR^5$, $-N(R^{25})C(O)R^5$, and $-N(R^{25})C(O)NR^{24}R^{25}$;

wherein each of the aryl, halo-substituted aryl, heteroaryl, cycloalkyl, and heterocycloalkyl groups of R^{21} is independently unsubstituted or substituted with one to four independently selected R^{23} moieties which can be the same or different, each R^{23} moiety being independently selected from the group of R^{23} moieties below,

or two R^{21} groups taken together with the carbon to which both R^{21} groups are attached is  ;

each R^{22} is independently selected from the group consisting of: halo, alkynyl, aryl, heteroaryl, $-OR^{24}$, -(C_1-C_6 alkyl)-OR^{24}, –CN, $-NO_2$, $-NR^{24}R^{25}$, $-C(O)R^{23}$, $-C(O)OR^{23}$, $-C(O)NR^{24}R^{25}$, $-S(O)_XNR^{24}R^{25}$, $-S(O)_XR^{23}$, $-CF_3$, $-OCF_3$, $-CF_2CF_3$, $-C(=NOH)R^{23}$, $-N(R^{24})S(O)_xR^{25}$, $-N(R^{24})C(O)R^{25}$, and $-N(R^{24})C(O)NR^{24}R^{25}$,

or two R^{22} groups taken together with the carbon to which both R^{22} groups are attached is  ;

each R^{23} is independently selected from the group consisting of H, hydroxyl, halo and alkyl;

each R^{24} is independently selected from the group consisting of H and alkyl;

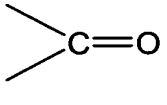
each R^{25} is independently selected from the group consisting of H, hydroxyl, alkyl, hydroxyalkyl, aryl, cycloalkyl, heteroaryl, $-NR^{24}R^{24}$, $-(C_1$ to C_6 alkyl)$NR^{24}N^{24}$, $-CF_3$ and $-S(O)_xR^{23}$;

each R^{26} is independently selected from the group consisting of H, hydroxyl, alkyl, hydroxyalkyl, aryl, cycloalkyl, heteroaryl and $-NR^3R^4$;

R^{27} is independently selected from the group consisting of heteroaryl, heterocycloalkyl and $-NR^{24}R^{25}$;

R^{30} is independently selected from the group consisting of H and R^{20} substituent groups above;

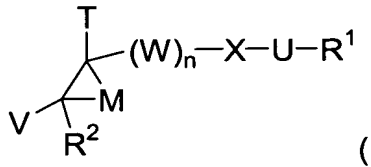
R^{40} is independently selected from the group consisting of H and R^{20} substituent groups above,

or R^{30} and R^{40}, taken together with the carbon to which R^{30} and R^{40} are attached, is  ;

with the proviso that at least one of V or T is selected from the group consisting of $-C(O)N(R^3)(OR^4)$, $-C(O)OR^3$ and $-C(O)NR^{24}R^{25}$.

69-72: (cancelled).

73. (new claim): A method of treating rheumatoid arthritis, osteoarthritis, periodontal disease, cancer or osteoporosis in a subject comprising: administering to the subject in need of such treatment a therapeutically effective amount of a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt, solvate or isomer thereof, wherein:

M is $-(C(R^{30})(R^{40}))_m-$, wherein m is 1;

T is selected from the group consisting of R^{21}-substituted alkyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, $-OR^3$, $-C(O)R^4$, $-C(O)OR^3$, $-C(O)NR^{24}R^{25}$, $-C(O)NR^{24}OR^3$, $-C(O)SR^3$, $-NR^{24}R^{25}$, $-NR^{25}C(O)R^4$, $-NR^{25}C(O)OR^3$, $-NR^{25}C(O)NR^{24}R^{25}$, $-NR^{25}C(O)NR^{24}OR^3$, $-SR^3$, $-S(O)_xNR^{24}R^{25}$, $-S(O)_xNR^{25}OR^3$, -CN, $-P(O)(R^{24})(OR^{24})$, $-P(O)(OR^{24})(OR^{24})$, $-C(R^4)(=N(OR^3))$, $-C(O)$-AA-$NR^{24}R^{25}$ and $-C(O)$-AA-$NR^{25}OR^3$,

wherein each of the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl and heteroaryl groups of T is independently unsubstituted or substituted with one to five independently selected R^{20} moieties which can be the same or different, each R^{20} moiety being independently selected from the group of R^{20} moieties below;

V is selected from the group consisting of alkyl, R^{21}-substituted alkyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, $-OR^3$, $-C(O)R^4$, $-(CR^{23}R^{24})_{n1}C(O)OR^3$, $-C(O)NR^{24}R^{25}$, $-(CR^{23}R^{24})_{n1}C(O)NR^{25}OR^3$, $-C(O)SR^3$, $-NR^{24}R^{25}$, $-NR^{25}C(O)R^4$, $-NR^{25}C(O)OR^3$, $-NR^{25}C(O)NR^{24}R^{25}$, $-NR^{25}C(O)NR^{24}OR^3$, $-SR^3$, $-S(O)_xNR^{24}R^{25}$, $-S(O)_xNR^{25}OR^3$, -CN, $-P(O)(R^{24})(OR^{24})$, $-P(O)(OR^{24})(OR^{24})$, $-C(R^4)(=N(OR^3))$, $-C(O)$-AA-$NR^{24}R^{25}$ and $-C(O)$-AA-$NR^{25}OR^3$,

wherein each of the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl and heteroaryl groups of V is independently unsubstituted or substituted with one to three independently selected R^{20} moieties which can be the same or different, each R^{20} moiety being independently selected from the group of R^{20}moieties below;

W is $-(CH_2)-$;

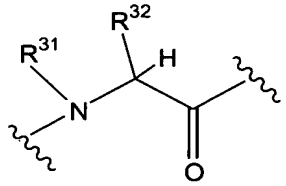
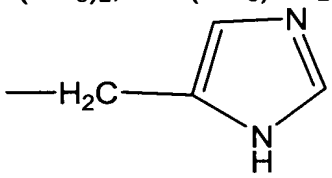
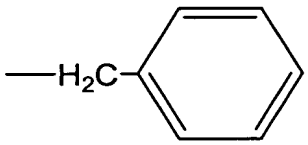
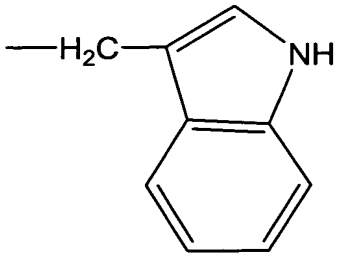
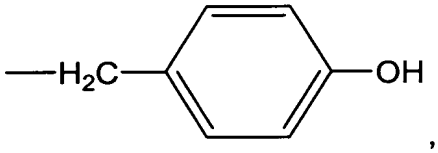
X is unsubstituted phenyl;

U is $-O-(CH_2)-$;

n is 0 to 2;

n1 is 0 to 2;

x is 0 to 2;

AA is  , wherein R^{31} and R^{32} are the same or different and are each independently selected from the group consisting of H, alkyl, cycloalkyl, aryl, heteroaryl, $-NR^{24}R^{25}$, $-(CH_2)_3NH(C=NH)NH_2$, $-CH_2C(O)NH_2$, $-CH_2C(O)OH$, $-CH_2SH$, $-CH_2S-SCH_2CH(NH_2)C(O)OH$, $-CH_2CH_2C(O)OH$, $-CH_2CH_2C(O)NH_2$, $-(CH_2)_4NH_2$, $-CH_2CH_2CH(OH)CH_2NH_2$, $-CH_2CH(CH_3)_2$, $-CH(CH_3)CH_2(CH_3)$, $-CH_2CH_2SCH_3$, $-CH_2OH$, $-CH(OH)(CH_3)$,  ,  ,  and  ,

or R^{31} and R^{32}, together with the N to which R^{31} is attached and the C to which R^{31} is attached, form a 5-membered ring which is unsubstituted or independently substituted with a hydroxyl group;

R^1 is selected from the group consisting of unsubstituted quinolyl, alkyl-substituted quinolyl and aryl-substituted quinolyl;

each R^2, R^4 and R^5 is the same or different and each is independently selected from the group consisting of H, halo, alkyl, R^{22}-substituted alkyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, $-OR^6$, $-C(O)R^7$, $-C(O)OR^6$, $-NR^{24}R^{25}$, $-NR^{24}C(O)R^{25}$, $-N(=C-O-NR^{24}R^{25})$, $-NR^{24}S(O)_2R^{25}$,

wherein each of the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl and heteroaryl groups of R^2, R^4 and R^5 is independently unsubstituted or substituted with one to four independently selected alkyl, R^{22}-substituted alkyl or R^{22} moieties which can be the same or

different, each R^{22} moiety being independently selected from the group of R^{22} moieties below;

each R^3 is the same or different and is independently selected from the group consisting of H, alkyl, R^{22}-substituted alkyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl, heteroaryl, $-OR^6$, $-C(O)R^7$, $-C(O)OR^6$, $-NR^{24}R^{25}$, $-NR^{24}C(O)R^{25}$, $-N(=C-O-NR^{24}R^{25})$ and $-NR^{24}S(O)_2R^{25}$,

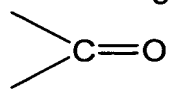
each of the cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, aryl and heteroaryl groups of R^3 is independently unsubstituted or substituted with one to four independently selected alkyl, R^{22}-substituted alkyl or R^{22} moieties which can be the same or different, each R^{22} moiety being independently selected from the group of R^{22} moieties below;

each R^6 is independently selected from the group consisting of H, alkyl and $-OCF_3$;

each R^7 is independently selected from the group consisting of H, alkyl, heteroaryl and $-CF_3$;

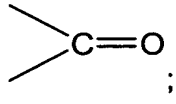
each R^{20} is independently selected from the group consisting of: alkyl, R^{21}-substituted alkyl, $-OR^3$, halo, -CN, $-NO_2$, $-NR^{24}R^{25}$, $-C(O)R^3$, $-C(O)OR^3$, $-C(O)NR^{24}R^{25}$, $-S(O)_xNR^{24}R^{25}$, $-S(O)_xR^5$, $-CF_3$, $-OCF_3$, $-CF_2CF_3$, $-C(=NOH)R^3$, aryl, halo-substituted aryl, heteroaryl, cycloalkyl, heterocycloalkyl, $-N(R^{25})S(O)_xR^5$, $-N(R^{25})C(O)R^5$, and $-N(R^{25})C(O)NR^{24}R^{25}$,

wherein each of the aryl, halo-substituted aryl, heteroaryl, cycloalkyl and heterocycloalkyl groups of R^{20} is independently unsubstituted or substituted with one to four independently selected R^{22} moieties which can be the same or different, each R^{22} moiety being independently selected from the group of R^{23} moieties below,

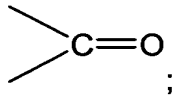
or two R^{20} groups taken together with the carbon to which both R^{20} groups are attached is  ;

R^{21} is one to three substituents independently selected from the group consisting of: $-OR^3$, halo, -CN, $-NO_2$, $-NR^{24}R^{25}$, $-C(O)R^3$, $-C(O)OR^3$, $-C(O)NR^{24}R^{25}$, $-S(O)_xNR^{24}R^{25}$, $-SO_xR^5$, $-CF_3$, $-OCF_3$, $-CF_2CF_3$, $-C(=NOH)R^3$, R^{23}-substituted alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, $-N(R^{25})S(O)_xR^5$, $-N(R^{25})C(O)R^5$, and $-N(R^{25})C(O)NR^{24}R^{25}$;

wherein each of the aryl, halo-substituted aryl, heteroaryl, cycloalkyl, and heterocycloalkyl groups of R^{21} is independently unsubstituted or substituted with one to four independently selected R^{23} moieties which can be the same or different, each R^{23} moiety being independently selected from the group of R^{23} moieties below,

or two R^{21} groups taken together with the carbon to which both R^{21} groups are attached is  ;

each R^{22} is independently selected from the group consisting of: halo, alkynyl, aryl, heteroaryl, $-OR^{24}$, $-(C_1\text{-}C_6$ alkyl)$-OR^{24}$, $-CN$, $-NO_2$, $-NR^{24}R^{25}$, $-C(O)R^{23}$, $-C(O)OR^{23}$, $-C(O)NR^{24}R^{25}$, $-S(O)_xNR^{24}R^{25}$, $-S(O)_xR^{23}$, $-CF_3$, $-OCF_3$, $-CF_2CF_3$, $-C(=NOH)R^{23}$, $-N(R^{24})S(O)_xR^{25}$, $-N(R^{24})C(O)R^{25}$, and $-N(R^{24})C(O)NR^{24}R^{25}$,

or two R^{22} groups taken together with the carbon to which both R^{22} groups are attached is  ;

each R^{23} is independently selected from the group consisting of H, hydroxyl, halo and alkyl;

each R^{24} is independently selected from the group consisting of H and alkyl;

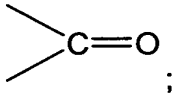
each R^{25} is independently selected from the group consisting of H, hydroxyl, alkyl, hydroxyalkyl, aryl, cycloalkyl, heteroaryl, $-NR^{24}R^{24}$, $-(C_1$ to C_6 alkyl)$NR^{24}N^{24}$, $-CF_3$ and $-S(O)_xR^{23}$;

each R^{26} is independently selected from the group consisting of H, hydroxyl, alkyl, hydroxyalkyl, aryl, cycloalkyl, heteroaryl and $-NR^3R^4$;

R^{27} is independently selected from the group consisting of heteroaryl, heterocycloalkyl and $-NR^{24}R^{25}$;

R^{30} is independently selected from the group consisting of H and R^{20} substituent groups above;

R^{40} is independently selected from the group consisting of H and R^{20} substituent groups above,

or R^{30} and R^{40}, taken together with the carbon to which R^{30} and R^{40} are attached, is  ;

with the proviso that at least one of V or T is selected from the group consisting of $-C(O)N(R^3)(OR^4)$, $-C(O)OR^3$ and $-C(O)NR^{24}R^{25}$.